

CLAIMS

1. A fatty acid-anticancer compound conjugate composition for administration to a subject, comprising at least one fatty acid-anticancer compound conjugate in a container for administration to a subject, wherein the amount of the fatty acid-anticancer compound in the container is at least about 10% greater than the maximum tolerated dose (MTD) for the unconjugated at least one anticancer compound.

2. The fatty acid-anticancer compound conjugate composition of claim 1, wherein the amount in the container is at least about 20% greater than the MTD for the unconjugated at least one anticancer compound.

3. The fatty acid-anticancer compound conjugate composition of claim 1, wherein the amount in the container is at least about 30% greater than the MTD for the unconjugated at least one anticancer compound.

4. The fatty acid-anticancer compound conjugate composition of claim 1, wherein the amount in the container is at least about 40% greater than the MTD for the unconjugated at least one anticancer compound.

5. The fatty acid-anticancer compound conjugate composition of claim 1, wherein the amount in the container is at least about 50% greater than the MTD for the unconjugated at least one anticancer compound.

6. The fatty acid-anticancer compound conjugate composition of claim 1, wherein the amount in the container is at least about 75% greater than the MTD for the unconjugated at least one anticancer compound.

7. The fatty acid-anticancer compound conjugate composition of claim 1, wherein the amount in the container is at least about 100% greater than the MTD for the unconjugated at least one anticancer compound.

8. The fatty acid-anticancer compound conjugate composition of claim 1, wherein the amount in the container is at least about 200% greater than the MTD for the unconjugated at least one anticancer compound.

9. The fatty acid-anticancer compound conjugate composition of claim 1, wherein the amount in the container is at least about 300% greater than the MTD for the unconjugated at least one anticancer compound.

10. The fatty acid-anticancer compound conjugate composition of claim 1, wherein the amount in the container is at least about 400% greater than the MTD for the unconjugated at least one anticancer compound.

11. The fatty acid-anticancer compound conjugate composition of claim 1, wherein the container is a container for intravenous administration.

12. The fatty acid-anticancer compound conjugate composition of claim 1, wherein the anticancer compound is a taxane.

13. The fatty acid-anticancer compound conjugate composition of claim 12, wherein the taxane is paclitaxel or docetaxel.

14. The fatty acid-anticancer compound conjugate composition of claim 1, wherein the conjugate is not encapsulated in a liposome.

15. The fatty acid-anticancer compound conjugate composition of claim 1, wherein the fatty acid is a C8-C26 unbranched, naturally occurring fatty acid.

16. The fatty acid-anticancer compound conjugate composition of claim 1, wherein the fatty acid is docosahexaenoic acid.

17. A method for treating a subject having an abnormal mammalian cell proliferative disorder, comprising administering to the subject a fatty acid-anticancer compound conjugate composition in an amount which is at least about 10% greater than the maximum tolerated dose (MTD) for the unconjugated at least one anticancer compound.

18. The method of claim 17, wherein the amount of the fatty acid-anticancer compound conjugate composition administered is at least about 20% greater than the MTD for the unconjugated at least one anticancer compound.

19. The method of claim 17, wherein the amount of the fatty acid-anticancer compound conjugate composition administered is at least about 30% greater than the MTD for the unconjugated at least one anticancer compound.

⁰A 20. The method of claim 17, wherein the amount of the fatty acid-anticancer compound conjugate composition administered is at least about 40% greater than the MTD for the unconjugated at least one anticancer compound.

⁶ 21. The method of claim 17⁵, wherein the amount of the fatty acid-anticancer compound conjugate composition administered is at least about 50% greater than the MTD for the unconjugated at least one anticancer compound.

⁰A 22. The method of claim 17, wherein the amount of the fatty acid-anticancer compound conjugate composition administered is at least about 75% greater than the MTD for the unconjugated at least one anticancer compound.

⁷ 23. The method of claim 17⁵, wherein the amount of the fatty acid-anticancer compound conjugate composition administered is at least about 100% greater than the MTD for the unconjugated at least one anticancer compound.

24. The method of claim 17, wherein the amount of the fatty acid-anticancer compound conjugate composition administered is at least about 200% greater than the MTD for the unconjugated at least one anticancer compound.

⁰A^b 25. The method of claim 17, wherein the amount of the fatty acid-anticancer compound conjugate composition administered is at least about 300% greater than the MTD for the unconjugated at least one anticancer compound.

26. The method of claim 17, wherein the amount of the fatty acid-anticancer compound conjugate composition administered is at least about 400% greater than the MTD for the unconjugated at least one anticancer compound.

⁸ 28. The method of claim 17⁵, wherein the anticancer compound is a taxane. .

29. The method of claim 28, wherein the taxane is paclitaxel or docetaxel.

30. The method of claim 17, wherein the conjugate is not encapsulated in a liposome.

⁰A 31. The method of claim 17, wherein the fatty acid is a C8-C26 unbranched, naturally occurring fatty acid.

32. The method of claim 17, wherein the fatty acid is docosahexaenoic acid.

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54. ~~The method of claim 48, wherein the subject is human.~~
55. ~~A method for administering a fatty acid-taxane conjugate to a subject in need of such treatment, comprising infusing the conjugate in fewer than 3 hours.~~
56. ~~The method of claim 55, wherein the conjugate is infused in 2 hours or less.~~

10 57. An injectable preparation of at least one fatty acid-taxane conjugate composition, comprising greater than about 6 mg/ml of the at least one fatty acid-taxane conjugate composition.

58. The injectable preparation of claim 57, wherein the preparation comprises greater than about 7 mg/ml of the at least one fatty acid-taxane conjugate composition..

59. The injectable preparation of claim 57, wherein the preparation comprises greater than about 8 mg/ml of the at least one fatty acid-taxane conjugate composition.

60. The injectable preparation of claim 57, wherein the preparation comprises greater than about 10 mg/ml of the at least one fatty acid-taxane conjugate composition.

61. The injectable preparation of claim 57, wherein the preparation comprises greater than about 15 mg/ml of the at least one fatty acid-taxane conjugate composition.

11 62. The injectable preparation of claim 57¹⁰, wherein the preparation comprises greater than about 20 mg/ml of the at least one fatty acid-taxane conjugate composition.

63. The injectable preparation of claim 57, wherein the preparation comprises greater than about 40 mg/ml of the at least one fatty acid-taxane conjugate composition.

64. The injectable preparation of claim 57, wherein the preparation comprises greater than about 60 mg/ml of the at least one fatty acid-taxane conjugate composition.

12 65. The injectable preparation of claim 57¹⁰, wherein the preparation comprises greater than about 80 mg/ml of the at least one fatty acid-taxane conjugate composition.

66. The injectable preparation of claim 57, wherein the preparation comprises greater than about 100 mg/ml of the at least one fatty acid-taxane conjugate composition.

67. ^b ~~A~~ The injectable preparation of claim 57, wherein the fatty acid is a C8-C26 unbranched, naturally occurring fatty acid.

68. ~~The injectable preparation of claim 67, wherein the fatty acid is docosohexaenoic acid.~~

69. ~~An injectable composition of at least one fatty acid-taxane conjugate, comprising less than about 0.3 mg/ml of the at least one fatty acid-taxane conjugate.~~

14 ~~70. A fatty acid-taxane conjugate composition, comprising greater than about 6 mg/ml of at least one fatty acid-taxane conjugate, and a surfactant.~~

71. ~~The fatty acid-taxane conjugate composition of claim 70, wherein the amount of the at least one fatty acid-taxane conjugate is greater than about 7 mg/ml.~~

72. ~~The fatty acid-taxane conjugate composition of claim 70, wherein the amount of the at least one fatty acid-taxane conjugate is greater than about 8 mg/ml.~~

73. ~~The fatty acid-taxane conjugate composition of claim 70, wherein the amount of the at least one fatty acid-taxane conjugate is greater than about 10 mg/ml.~~

74. ~~The fatty acid-taxane conjugate composition of claim 70, wherein the amount of the at least one fatty acid-taxane conjugate is greater than about 15 mg/ml.~~

15 ~~75. The fatty acid-taxane conjugate composition of claim 70¹⁴, wherein the amount of the at least one fatty acid-taxane conjugate is greater than about 20 mg/ml.~~

76. ~~The fatty acid-taxane conjugate composition of claim 70, wherein the amount of the at least one fatty acid-taxane conjugate is greater than about 40 mg/ml.~~

77. ~~The fatty acid-taxane conjugate composition of claim 70, wherein the amount of the at least one fatty acid-taxane conjugate is greater than about 60 mg/ml.~~

16 ~~78. The fatty acid-taxane conjugate composition of claim 70¹⁴, wherein the amount of the at least one fatty acid-taxane conjugate is greater than about 80 mg/ml.~~

79. ~~The fatty acid-taxane conjugate composition of claim 70, wherein the amount of the at least one fatty acid-taxane conjugate is greater than about 100 mg/ml.~~

80. ~~The fatty acid-taxane conjugate composition of claim 70, wherein the fatty acid is a C8-C26 unbranched, naturally occurring fatty acid.~~

^{A⁰} 81. The fatty acid-taxane conjugate composition of claim 80, wherein the fatty acid is docosohexaenoic acid

^{A⁰} 82. The fatty acid-taxane conjugate composition of claim 70, wherein the surfactant is Cremophor EL or EL-P.

^{A⁰} 83. The fatty acid-taxane conjugate composition of claim 82, wherein the concentration of Cremophor is between about 9.6% and about 49.7% (vol/vol).

¹⁸ 84. A fatty acid-taxane conjugate composition, comprising at least one fatty acid-taxane conjugate and a surfactant, wherein the ratio of the weight of the at least one fatty acid-taxane conjugate and volume of the surfactant is at least about 50 mg/ml.

⁸⁵ 85. The fatty acid-taxane conjugate composition of claim 84, wherein the ratio of the weight of the at least one fatty acid-taxane conjugate and volume of the surfactant is at least about 60 mg/ml.

⁸⁶ 86. The fatty acid-taxane conjugate composition of claim 84, wherein the ratio of the weight of the at least one fatty acid-taxane conjugate and volume of the surfactant is at least about 70 mg/ml.

^{A⁰} 87. The fatty acid-taxane conjugate composition of claim 84, wherein the ratio of the weight of the at least one fatty acid-taxane conjugate and volume of the surfactant is at least about 80 mg/ml.

⁸⁸ 88. The fatty acid-taxane conjugate composition of claim 84, wherein the ratio of the weight of the at least one fatty acid-taxane conjugate and volume of the surfactant is at least about 90 mg/ml.

¹⁹ 89. The fatty acid-taxane conjugate composition of claim 84, wherein the ratio of the weight of the at least one fatty acid-taxane conjugate and volume of the surfactant is at least about 100 mg/ml.

⁹⁰ 90. The fatty acid-taxane conjugate composition of claim 84, wherein the surfactant is Cremophor EL or EL-P.

^{A⁰} 91. The fatty acid-taxane conjugate composition of claim 84, wherein the fatty acid is a C8-C26 unbranched, naturally occurring fatty acid.

92. The fatty acid-taxane conjugate composition of claim 91, wherein the fatty acid is docosaheptaenoic acid.

A 93. The fatty acid-taxane conjugate composition of claim 84, wherein the taxane is paclitaxel or docetaxel.

24 94. The fatty acid-taxane conjugate composition of claim ¹⁸84, further comprising a solvent.

0 95. The fatty acid-taxane conjugate composition of claim 94, wherein the solvent is ethanol.

A 96. The fatty acid-taxane conjugate composition of claim 95, wherein the solvent and the surfactant are present in a ratio of about 1:1.

22 97. A fatty acid-taxane conjugate composition, comprising at least one fatty acid-taxane conjugate and a solvent, wherein the ratio of the weight of the at least one fatty acid-taxane conjugate and volume of the solvent is at least about 42 mg/ml.

98. The fatty acid-taxane conjugate composition of claim 97, wherein the ratio of the weight of the at least one fatty acid-taxane conjugate and volume of the solvent is at least about 50 mg/ml.

99. The fatty acid-taxane conjugate composition of claim 97, wherein the ratio of the weight of the at least one fatty acid-taxane conjugate and volume of the solvent is at least about 60 mg/ml.

100. The fatty acid-taxane conjugate composition of claim 97, wherein the ratio of the weight of the at least one fatty acid-taxane conjugate and volume of the solvent is at least about 70 mg/ml.

23 101. The fatty acid-taxane conjugate composition of claim ²²97, wherein the ratio of the weight of the at least one fatty acid-taxane conjugate and volume of the solvent is at least about 80 mg/ml.

A 102. The fatty acid-taxane conjugate composition of claim 97, wherein the ratio of the weight of the at least one fatty acid-taxane conjugate and volume of the solvent is at least about 100 mg/ml.

103. The fatty acid-taxane conjugate composition of claim 97, wherein the solvent is Cremophor EL.

104. The fatty acid-taxane conjugate composition of claim 97, wherein the fatty acid is a C8-C26 unbranched, naturally occurring fatty acid.

105. The fatty acid-taxane conjugate composition of claim 104, wherein the fatty acid is docosahexaenoic acid.

106. The fatty acid-taxane conjugate composition of claim 97, wherein the taxane is paclitaxel or docetaxel.

107. The fatty acid-taxane conjugate composition of claim 97, further comprising a surfactant.

108. The fatty acid-taxane conjugate composition of claim 107, wherein the surfactant is Cremophor.

109. The fatty acid-taxane conjugate composition of claim 108, wherein the solvent and the surfactant are present in a ratio of about 1:1.

110. A fatty acid-taxane conjugate composition, comprising at least about 37 mg/ml of at least one fatty acid-taxane conjugate.

111. The fatty acid-taxane conjugate composition of claim 110, wherein the amount of the at least one fatty acid-taxane conjugate is least about 40 mg/ml.

112. The fatty acid-taxane conjugate composition of claim 110, wherein the amount of the at least one fatty acid-taxane conjugate is least about 50 mg/ml.

113. The fatty acid-taxane conjugate composition of claim 110, wherein the amount of the at least one fatty acid-taxane conjugate is least about 60 mg/ml.

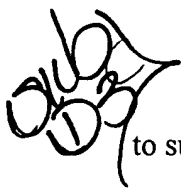
114. The fatty acid-taxane conjugate composition of claim 110, wherein the amount of the at least one fatty acid-taxane conjugate is least about 80 mg/ml.

115. The fatty acid-taxane conjugate composition of claim 110, wherein the amount of the at least one fatty acid-taxane conjugate is least about 100 mg/ml.

116. The fatty acid-taxane conjugate composition of claim 110, wherein the fatty acid is a C8-C26 unbranched, naturally occurring fatty acid.

117. The fatty acid-taxane conjugate composition of claim 110, wherein the fatty acid is docosahexaenoic acid.

33. A kit for administration of a fatty acid-anticancer compound conjugate composition to a subject, comprising

 a container containing at least one fatty acid-anticancer compound conjugate, and instructions for administering the at least one fatty acid-anticancer compound conjugate to subject in need of such treatment in an amount which is at least about 10% greater than the maximum tolerated dose (MTD) for the unconjugated at least one anticancer compound.

34. The kit of claim 33, wherein the amount of the at least one fatty acid-anticancer compound conjugate is at least about 20% greater than the MTD for the unconjugated at least one anticancer compound.

35. The kit of claim 33, wherein the amount of the at least one fatty acid-anticancer compound conjugate is at least about 30% greater than the MTD for the unconjugated at least one anticancer compound.

36. The kit of claim 33, wherein the amount of the at least one fatty acid-anticancer compound conjugate is at least about 40% greater than the MTD for the unconjugated at least one anticancer compound.

37. The kit of claim 33, wherein the amount of the at least one fatty acid-anticancer compound conjugate is at least about 50% greater than the MTD for the unconjugated at least one anticancer compound.

38. The kit of claim 33, wherein the amount of the at least one fatty acid-anticancer compound conjugate is at least about 75% greater than the MTD for the unconjugated at least one anticancer compound.

39. The kit of claim 33, wherein the amount of the at least one fatty acid-anticancer compound conjugate is at least about 100% greater than the MTD for the unconjugated at least one anticancer compound.

40. The kit of claim 33, wherein the amount of the at least one fatty acid-anticancer compound conjugate is at least about 200% greater than the MTD for the unconjugated at least one anticancer compound.

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41. The kit of claim 33, wherein the amount of the at least one fatty acid-anticancer compound conjugate is at least about 300% greater than the MTD for the unconjugated at least one anticancer compound.

42. The kit of claim 33, wherein the amount of the at least one fatty acid-anticancer compound conjugate is at least about 400% greater than the MTD for the unconjugated at least one anticancer compound.

43. The kit of claim 33, wherein the at least one fatty acid-anticancer compound conjugate is a taxane. .

44. The kit of claim 43, wherein the taxane is paclitaxel or docetaxel.

45. The kit of claim 33, wherein the conjugate is not encapsulated in a liposome.

46. The kit of claim 33, wherein the fatty acid is a C8-C26 unbranched, naturally occurring fatty acid.

47. The kit of claim 33, wherein the fatty acid is docosohexaenoic acid.

48. A method for increasing the therapeutic index of anticancer compounds in a subject, comprising

conjugating a fatty acid to an anticancer compound to form a fatty acid-anticancer compound conjugate; and

administering the fatty acid-anticancer compound conjugate to the subject, whereby the therapeutic index of the anticancer compound is improved relative to non-conjugated formulations of the anticancer compound.

49. ~~The method of claim 48, wherein the anticancer compound is a taxane.~~

50. The method of claim 49, wherein the taxane is paclitaxel or docetaxel.

51. The method of claim 48, wherein the conjugate is not encapsulated in a liposome.

52. The method of claim 48, wherein the fatty acid is a C8-C26 unbranched, naturally occurring fatty acid.

53. The method of claim 52, wherein the fatty acid is docosohexaenoic acid.

118. The fatty acid-taxane conjugate composition of claim 110, wherein the taxane is paclitaxel or docetaxel.

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